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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/991,971	11/26/2001	Markku Ahotupa	2630-113	8814

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ROTHWELL, FIGG, ERNST & MANBECK, P.C.
1425 K STREET, N.W.
SUITE 800
WASHINGTON, DC 20005

EXAMINER	
HUYNH, PHUONG N	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 10/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/991,971	AHOTUPA ET AL.	
	Examiner	Art Unit	
	Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,17 and 18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,17 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submissions filed on 8/18/04 and 10/7/04 have been entered.

2. Claims 1-6 and 17-18 are pending and are being acted upon in this Office Action.

3. The abstract of the disclosure is objected to because the abstract is not limited to a single paragraph. Correction is required. See MPEP § 608.01(b).
Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to **a single paragraph on a separate sheet within the range of 50 to 150 words**. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1 and 4 are rejected under 35 U.S.C. 112, first paragraph, containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection.**

The "the overactivity that is inhibited is lifespan controlled by Fas-mediated apoptosis" in Claim 1 represents a departure from the specification and the claims as originally filed. The specification on page 10 line 5 and Figure 2 discloses hydroxymatairesinol, matairesinol or enterolactone increases Fas-induced apoptosis in Jurkat T cells from 20 % (Fas alone) to 50-60%. The claim as written suggests that the hydroxymatairesinol, matairesinol or enterolactone inhibits

rather than increases Fas-induced apoptosis in T cells. Further, the term "lifespan" has no support in the specification as filed.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

7. Claim 1 is rejected under 35 U.S.C. 102(a) as being anticipated by Yesilada et al (Cytokine 13(6): 359-364, March 2001; PTO 892).

Yesilada *et al* teach a method of inhibiting the overactivity of phagocyte or lymphocyte such as peripheral blood of an individual which inherently contains lymphocytes and macrophage by administering these cells to a lignan such as matairesinol (See Figure 1, compound 14, in particular). The reference matairesinol inhibits TNF alpha production by the reference cells (See Table 3, compound 14, Table 5, compound 14, page 361, col. 2, in particular). The reference matairesinol found in aerial parts or roots of Daphne oleokes Schreber have been used in Turkish folk medicine for treatment of rheumatoid arthritis by inhibiting TNF alpha production (See page 359, in particular). The reference in vitro data extends the in vivo effect of the remedy. Thus, the reference teachings anticipate the claimed invention.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was

made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1-6, 17 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,451,849 B1 (filed March 30, 1999) in view of Morikawa *et al* (J. Pharm Pharmacol 44(10): 859-61, Oct 1992; PTO 892) or Yesilada et al (Cytokine 13(6): 359-364, March 21, 2001; PTO 892) or Hirano et al (Life Science 55(13): 1061-1069, 1994; PTO 892).

The '849 patent teaches a method of administering to an individual an effective amount of lignan such as hydroxymatairesinol that has the same structure as shown in claim 1 (See entire document, col. 2, in particular). The reference hydroxymatairesinol from plant is converted to enterolactone by gut microflora (See col. 2, lines 19- 20, in particular). The reference method is useful in inhibiting the over activity of cell such as a decrease in LDL oxidation (See col. 6, lines 27-30, Table 3, in particular), inhibition of lipid peroxidation (See col. 7, lines 4-5, Table 2, in particular) and superoxide anion scavenging (See col. 7, line 44, in particular). The '849 patent teaches hydroxymatairesinol is useful for treating cancers (See abstract, in particular).

The invention in claim 1 differs from the teachings of the references only in that the method wherein the phagocytes are neutrophils, the lignan is enterolactone or the phagocytes are macrophages and the lignan is enterolactone or hydroxymatairesinol.

Morikawa *et al* teach enterolactone inhibits fMLP induced oxidative bursts such as superoxide production by human polymorphonuclear leukocytes (neutrophils) (See abstract, in particular).

Yesilada *et al* teach matairesinol is a lignan having a structure identical to the claimed matairesinol (See page 362, compound 14, in particular) that inhibits over activity of phagocytes such as TNF alpha production by macrophages, which are cells of myeloid origin, and peripheral blood lymphocytes (See page 360, col. 1, compound 14, page 361, col. 2, Table 3, Table 5, in particular). Yesilada et al teach that matairesinol is useful for inhibiting over activity of phagocytes in rheumatoid arthritis, and confirms that lignans from the aerial parts or roots of D. oleoides ssp. Oleoides which have been used in Turkish folk medicine for treatment of rheumatoid pain (See page 361, col. 2, last par, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made that the inhibitory effect of hydroxymatairesinol and its metabolites such as enterolactone and matairesinol on lipid peroxidation as taught by the '849 patent is mediated by

cell type such as neutrophils as taught by Morikawa *et al* and macrophage as taught by Yesilada *et al.* From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because Yesilada et al teach that matairesinol is useful for inhibiting over activity of phagocytes in rheumatoid arthritis, and confirms that lignans from the aerial parts or roots of D. oleoides ssp. Oleoides which have been used in Turkish folk medicine for treatment of rheumatoid pain (See page 361, col. 2, last par, in particular). Morikawa *et al* teach enterolactone inhibits fMLP induced oxidative bursts such as superoxide production by human polymorphonuclear leukocytes (neutrophils) (See abstract, in particular). The '849 patent teaches hydroxymatairesinol is useful for treating cancers (See abstract, in particular).

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh "NEON" whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Friday from 9:00 am to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The IFW official Fax number is (703) 872-9306.

13. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Phuong N. Huynh, Ph.D.
Patent Examiner
Technology Center 1600
October 15, 2004

Christina Chan
CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600